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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/525,015	02/17/2005	Noboru Yamaji	Q86324	5025

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2100 PENNSYLVANIA AVE. NW
WASHINGTON, DC 20037-3213

EXAMINER	
KOSAR, ANDREW D	

ART UNIT	PAPER NUMBER
1654	

MAIL DATE	DELIVERY MODE
04/08/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/525,015	YAMAJI ET AL.	
	Examiner	Art Unit	
	Andrew D. Kosar	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *31 January 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *16 and 18-21* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *16 and 18-21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination

Applicant's request for reconsideration of the finality of the rejection of the last Office action is persuasive and, therefore, the finality of that action is withdrawn.

Applicant has introduced new claims 19-21. Claim 18 is indicated as 'previously presented', however it is clearly amended, now reciting new embodiments- arthrosteitis and rheumatoid arthritis which were not previously present in claim 18. In the interest of compact prosecution and in accordance with MPEP § 714.03, the examiner has accepted the amendments, as it is clear to the examiner which text has been added to claim 18. This does not absolve Applicant from providing proper amendments in the future.

In accordance with MPEP § 706.07(d) this action is made FINAL. Applicant is reminded that MPEP § 706.07(a) states, "A second or any subsequent action on the merits in any application or patent involved in reexamination proceedings should not be made final if it includes a rejection, on prior art not of record, of any claim amended to include limitations which should reasonably have been expected to be claimed. See MPEP § 904 *et seq.* However, note that *an examiner cannot be expected to foresee whether or how an applicant will amend a claim to overcome a rejection except in very limited circumstances* (e.g., where the examiner suggests how applicant can overcome a rejection under 35 U.S.C. 112, second paragraph)". Here, the examiner did not suggest incorporating new embodiments to claim 18, nor did the examiner suggest new claims 19-21 be presented. Furthermore, the examiner could not foresee that Applicant would amend claim 18 to incorporate previously rejected embodiments of now-cancelled claims or reasonably expect the new claims which are now presented.

Response to Amendment / Arguments

Applicant's amendments and arguments filed January 31, 2008 are acknowledged and have been fully considered. Any rejection and/or objection not specifically addressed is herein withdrawn. Applicant has introduced new claims 19-21, necessitating new grounds of rejection below. The rejections of claims 11, 13-15 and 17 are withdrawn as moot, as the claims are no longer pending.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 18-21 are rejected under 35 U.S.C. 102(b) as being anticipated by KAMMER (PTO-1449, 6/24/05).

Previously, Applicant provided references and argued that the cause of RA was not understood (discussed in Office Action of 11/8/07, spanning pages 2 and 3), thus one would not have distinguished the cause of RA, but rather treated the condition irrespective of the underlying cause. Here, Applicant is claiming the treatment of RA and arthrosteitis, and as discussed previously, Kammer specifically *claims* treating rheumatoid arthritis (herein 'RA') with the HDACi (referenced below). Since ACEM is an underlying condition/feature of RA, in treating RA, one is necessarily inhibiting ACEM degradation and the associated inflammation (arthrosteitis). Applicant did not argue or dispute that Kammer teaches- and claims- treating RA with HDACi (below), but rather argued that it was not understood what was believed to be the underlying mechanism, however in treating RA with the HDACi, one is inherently practicing the instantly claimed invention. Applicant is reminded that the inherent feature and necessary result,

here the underlying cause of RA, need not be recognized at the time of the invention and occurs when practicing the method of Kammer (cf. MPEP § 2112 (II), citing *Toro Co. v. Deere & Co.*, 355 F.3d 1313, 1320, 69 USPQ2d 1584, 1590 (Fed. Cir. 2004), "[T]he fact that a characteristic is a necessary feature or result of a prior-art embodiment (that is itself sufficiently described and enabled) is enough for inherent anticipation, even if that fact was unknown at the time of the prior invention.").

The instant claims are drawn generally to administering HDACi to treat arthrosteitis, rheumatoid arthritis (herein 'RA') or osteoarthritis caused by ACEM.

The teachings of Kammer have been presented previously (*see* Office Action 4/20/06, pages 11-12). Kammer teaches a method of treating RA with a histone hyperacetylating agent (claim 10). In looking to the specification for the preferred embodiments of the histone hyperacetylating agent usable in the method, the specification provides that HDACi are the preferred compounds (citing WO 97/11366), providing exemplary HDACi usable in the methods, including trichostatin A, SBHA, SAHA, apicidin (e.g *Specification pages 6-8*) and specifically embodies in the claims (e.g. claims 3-9) trichostatin A, trapoxin A, FK228 (FR901228) and MS-275 (MS-27-275). Kammer teaches that the compounds are preferably administered at 1 μmol/kg to 50 μmol/kg, more preferably at 22 μmol/kg to 33 μmol/kg for oral and i.v. administration, thus being of an overlapping, if not commensurate scope of the instantly disclosed preferred dosages and thus would have the same IC_{50} if tested as claimed in new claim 21. Further, as presented by Applicant, the underlying cause of RA was not understood, and thus one would not have simply treated RA regardless of the underlying condition. Additionally, as

presented previously, it is noted that Applicant admits in the instant specification that Kammer teaches treating RA with HDACi (spanning pages 6-7 of the instant specification).

Claims 16 and 18-21 are/remain rejected under 35 U.S.C. 102(b) as being anticipated by WATKINS (WO 02/30879 A2).

Applicant argues that, "Watkins does not have Examples or an explanation other than the disclosure [diseases/conditions spanning pages 110-111] as to whether the HDAC inhibitors can be used for inflammatory disease and osteoarthritis." (Remarks, page 5). Applicant further provides the cited references from Watkins and argues that the teachings therein do not support the rejection, concluding that Watkins is not enabling for treating inflammatory diseases or osteoarthritis. (Remarks, page 6).

Respectfully, the examiner disagrees. Watkins clearly and unambiguously states that HDAC inhibitors (e.g. Trichostatin A) were known to be used in the treatment of conditions including osteoarthritis and RA. Further, Applicant has provided no evidence to rebut the explicit teaching that Watkins provides- RA and osteoarthritis are treatable with HDAC inhibitors, but rather provides references cited by Watkins to assert it is not enabled. The examiner disagrees with Applicant's assertions as to what these references provide in the way of teachings, in that Watkins does not explicitly present the two cited references as being specific to RA and/or osteoarthritis and as interpreted by the examiner provide fundamental science regarding general cellular inflammation. Absent a specific statement in Watkins that those references are explicitly cited to show treating RA/osteoarthritis is the reason they are cited, one cannot conclude that was the intent of Watkins. In contrast, the examiner has previously provided sufficient evidence that RA was treatable with HDAC inhibitors (e.g. Kammer, above).

Applicant is reminded that MPEP § 2121 states, "When the reference relied on expressly anticipates or makes obvious all of the elements of the claimed invention, the reference is presumed to be operable. Once such a reference is found, the burden is on applicant to provide facts rebutting the presumption of operability. *In re Sasse*, 629 F.2d 675, 207 USPQ 107 (CCPA 1980)." Here, Applicant has provided no facts to rebut the presumption of operability, and in direct contrast, clearly provides evidence in the instant disclosure that HDAC inhibitors have been used for RA and osteoarthritis (above, and Page 6, specification).

The instant claims are presented *supra*. Watkins teaches that HDACi are well known for treating osteoarthritis and RA (e.g. page 111, lines 1 and 2) and teaches a myriad of HDACi, including those instantly claimed (e.g. trichostatin A and SAHA, page 4, page 111). Thus, in treating osteoarthritis or RA and the associated inflammation (arthrosteitis) with the HDACi, one is inherently inhibiting/treating the underlying conditions/cause, e.g. ACEM degradation. Further, as discussed above, the underlying cause of RA was not understood at the time of the invention and thus one would not distinguish the cause and simply treat the condition with the compound.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after

the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Andrew D. Kosar whose telephone number is (571)272-0913. The examiner can normally be reached on Monday - Friday 08:00 - 16:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia J. Tsang can be reached on (571)272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Andrew D Kosar/
Primary Examiner, Art Unit 1654